

## The evolving role of lyophilized plasma in remote damage control resuscitation in the French Armed Forces Health Service

Anne Sailliol, Christophe Martinaud, Andrew P. Cap, Corinne Civadier, Benoit Clavier, Anne-Virginie Deshayes, Anne-Christine Mendes, Thomas Pouget, Nicolas Demazeau, Marine Chueca, François-Régis Martelet, and Sylvain Ausset

Freeze-dried plasma was developed by the US Army for the resuscitation of combat casualties during World War II. The French Military Blood Institute began producing French lyophilized plasma (FLYP) in 1949, in accordance with French blood product guidelines. Since 2010, a photochemical pathogen inactivation process has been implemented to reduce the remaining transfusion-related infectious risk. All quality controls for this procedure verify that the hemostatic properties of FLYP are conserved. FLYP is compatible with all blood types, can be stored at room temperature for 2 years, and its reconstitution requires less than 6 minutes. As a result, FLYP allows quick delivery of all the coagulation proteins and the application of a 1:1 ratio of FLYP and red blood cells in the context of a massive transfusion. Hemovigilance data collected in France since 1994 have included FLYP. Results indicate no reporting of infection related to the use of FLYP. Clinical monitoring with a focus on hemostasis was implemented in 2002 and expanded in 2010. The data, obtained from overseas operations, confirmed the indications, the safety and the clinical efficacy of FLYP. Further research is needed to determine specific indications for FLYP in the therapeutic management of civilian patients with severe hemorrhage.

### OVERVIEW OF THE CENTRE DE TRANSFUSION SANGUINE DES ARMÉES (CTSA) AND FREEZE-DRIED PLASMA PRODUCTION

The French Military Blood Institute (Centre de Transfusion Sanguine des Armées [CTSA]) was created after World War II by Jean Juliard, a military physician. The primary mission of this institute has been to support transfusion in overseas operations and in military medical centers. This includes production of blood products, provision of transfusion advice 24 hours a day, hemovigilance, and blood traceability.<sup>1</sup> In addition, CTSA is an immunohematology laboratory, a training center for transfusion practices in overseas operations, an institute of cell and tissue therapy, and a blood and skin research institute.

### HISTORY OF FRENCH FREEZE-DRIED PLASMA<sup>2</sup>

In 1945, Jean Juliard decided to produce freeze-dried plasma (FDP) at his center following the successful use of the FDP that was produced by the United States during

From the Centre de Transfusion Sanguine des Armées; and the Fédération de Biologie Clinique, and the Département d'Anesthésie et de Réanimation, HIA Percy, Clamart, France; and the US Army Institute of Surgical Research, Fort Sam Houston, Texas.

*Address reprint requests to:* Anne Sailliol, Directrice du CTSA, 1 rue Raoul Batany, 92140 Clamart CEDEX, France; e-mail: anne.sailliol@wanadoo.fr; anne.sailliol@sante.defense.gouv.fr.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Department of the Army or the U.S. Department of Defense.

doi: 10.1111/trf.12038

TRANSFUSION 2013;53:65S-71S.

<b>Report Documentation Page</b>			Form Approved OMB No. 0704-0188	
<p>Public reporting burden for the collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to a penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.</p>				
1. REPORT DATE <b>01 JAN 2013</b>	2. REPORT TYPE <b>N/A</b>	3. DATES COVERED <b>-</b>		
<b>4. TITLE AND SUBTITLE</b> <b>The evolving role of lyophilized plasma in remote damage control resuscitation in the French Armed Forces Health Service</b>			5a. CONTRACT NUMBER	
			5b. GRANT NUMBER	
			5c. PROGRAM ELEMENT NUMBER	
<b>6. AUTHOR(S)</b> <b>Sailliol A., Martinaud C., Cap A. P., Civadier C., Clavier B., Deshayes A. V., Mendes A. C., Pouget T., Demazeau N., Chueca M.,</b>			5d. PROJECT NUMBER	
			5e. TASK NUMBER	
			5f. WORK UNIT NUMBER	
<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b> <b>United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX</b>			8. PERFORMING ORGANIZATION REPORT NUMBER	
<b>9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b>			10. SPONSOR/MONITOR'S ACRONYM(S)	
			11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
<b>12. DISTRIBUTION/AVAILABILITY STATEMENT</b> <b>Approved for public release, distribution unlimited</b>				
<b>13. SUPPLEMENTARY NOTES</b>				
<b>14. ABSTRACT</b>				
<b>15. SUBJECT TERMS</b>				
<b>16. SECURITY CLASSIFICATION OF:</b> a. REPORT <b>unclassified</b>			<b>17. LIMITATION OF ABSTRACT</b> <b>UU</b>	<b>18. NUMBER OF PAGES</b> <b>7</b>
b. ABSTRACT <b>unclassified</b>				
c. THIS PAGE <b>unclassified</b>				
<b>19a. NAME OF RESPONSIBLE PERSON</b>				

World War II. In 1950, the CTSA became the first European center of FDP production. During the Indochina war, almost 40,000 units were delivered to support French military operations. From 1985 to 1991, production was suspended to prevent the spread of HIV infection from the pooled plasma used in FDP. Production restarted in 1991 at the time of the Gulf War and continues to the present. In 1994, when a formal hemovigilance program began in France, FDP production entered a new phase as an effort licensed by the French blood agency to support overseas operations. French lyophilized plasma (FLYP) is manufactured from pooled fresh frozen plasma (FFP) obtained from less than 11 donors by apheresis. FLYP has been leukoreduced since 2003. As of 2010, plasma from women with a history of pregnancy has been tested for anti-human leukocyte antigen (HLA) antibodies and excluded if positive. Also beginning in 2010, FLYP has been secured with the amotosalen and ultraviolet light process (Cerus Intercept technology, Cerus Corporation, Concord, CA) to inactivate RNA/DNA pathogens. In 2011, FLYP was authorized by the French Agency for Sanitary Safety of Health Products (AFSSAPS) for civilian use in austere settings, or when thawed plasma is unavailable in emergency situations. No adverse events, including transfusion-related acute lung injury, have been reported since 1994, when the French hemovigilance program began. In particular, no viral seroconversion has been reported in patients transfused with FLYP. Since 2003, the CTSA has assessed the use of FLYP in overseas settings, with a focus on clinical and (since 2010) biological efficacy and safety. French military experience suggests that early transfusion of FLYP, combined with red blood cells (RBCs) in a 1:1 ratio, is associated with a survival advantage by prevention or correction of coagulation disorders without causing adverse effects.<sup>3,4</sup>

### FRENCH MILITARY TRANSFUSION GUIDELINES<sup>5</sup>

The French Armed Forces Health Service regularly updates its transfusion policies for overseas operations according to its previous experience and the best available evidence from the medical literature.<sup>6,7</sup> Hemorrhagic shock is a frequent cause of death in combat and the principal cause of preventable death. This is thought to be due to the early coagulopathy of trauma, which is associated with increased mortality and blood product requirements. The French military advocates emergency treatment of severely bleeding combat casualties with the following interventions: tourniquets applied immediately in the field, hemo-

static dressings, tranexamic acid within the first 3 hours, transfusion of FLYP and RBCs in a 1:1 ratio, fresh whole blood (FWB) use, correction of acidosis with bicarbonate infusion, aggressive rewarming, calcium infusion to treat citrate toxicity, fibrinogen supplementation to maintain a minimum level of 1.5 g/L, judicious use of rFVIIa,<sup>8</sup> and damage control surgery.

In addition, at Role 2 and 3 hospitals, laboratory tests including blood group typing, Quick time (prothrombin time [PT]), fibrinogen, and hemoglobin levels are performed on blood samples drawn on admission from hemorrhaging casualties.

### BLOOD SUPPLY TO OVERSEAS OPERATIONS<sup>9</sup>

In 2012, the French army was engaged in several overseas operations around the world, and all of them were supplied with blood products (Fig. 1). In Djibouti, the French military maintains a Role 2 or 3 military treatment facility where FLYP is used as the sole therapeutic plasma product for all indications including obstetric hemorrhage, hemophilia-related bleeding,<sup>10</sup> envenomation, hemorrhagic trauma, and even the treatment of hemolytic-uremic syndrome. In overseas contingency operations, blood products are delivered to all medical facilities staffed by medical doctors (Fig. 2). Before 2012, only Role 2 and 3, and medical evacuation (MEDEVAC) between overseas and France (Role 4) were supplied with FLYP. Currently, when evacuation times are longer than 3 hours, FLYP is positioned in Role 1 and in MEDEVAC platforms flying between Role 1 and Role 2 or 3, along with FWB collection kits. Platelets are sent only with MEDEVAC from France. RBCs are packed in insulated containers with

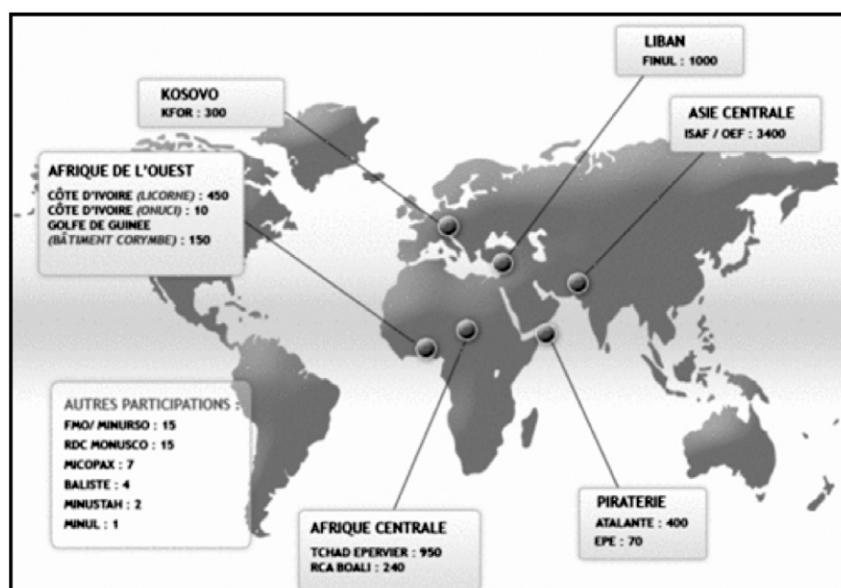


Fig. 1. Overseas operations in 2012.

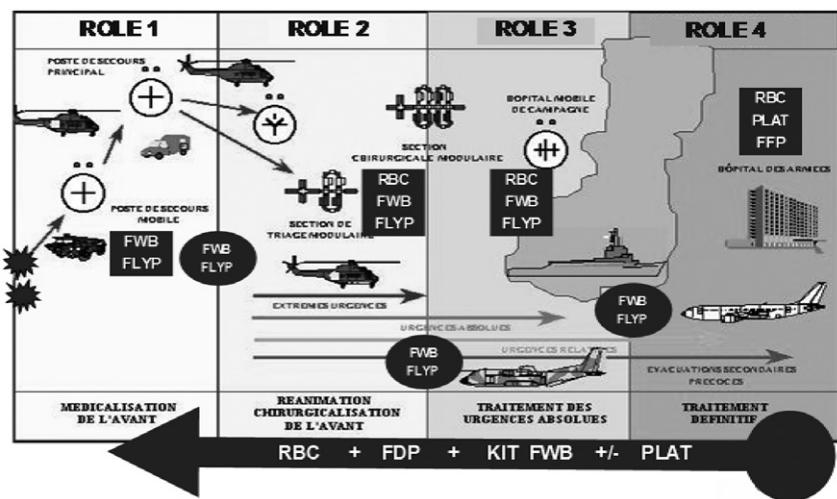


Fig. 2. Blood chain to supply overseas operations.

TABLE 1. Characteristic controls performed on each new batch of FLYP

Test	Reference range
Hemolysin	None
Anti-A	<1/64
Anti-B	<1/64
Irregular antibodies	None
Fibrinogen factor	≥2 g/L
Factor VIII	≥0.5 IU/mL
Amotosalen residual	<2 µM
Proteins	≥50 g/L
Moisture	<2%
Reconstitution time	<180 sec

eutectics and a temperature recorder. FLYP is transported at room temperature (between 2 and 25°C). On the battlefield, RBCs are stored in a deployed blood bank. We deliver two types of FWB collection kits: one for Roles 2 and 3 with one bag to collect blood and five tubes for blood samples, and another for Role 1 with all components necessary for collection, ABO compatibility, and infectious disease testing (HIV and hepatitis C virus [HCV]). In order to decrease infection risk, donors are prescreened before overseas deployment.

## FLYP

### FLYP production<sup>11</sup>

The CTSA has developed expertise in production and use of lyophilized plasma since 1949. All donors are volunteers and undergo rigorous medical selection to ensure efficacy (with appropriate factor levels) and safety. The following tests are performed on all blood products: hemoglobin, ABO-Rh-Kell grouping, HIV 1 and 2 antibodies and nucleic acid testing (NAT), HCV antibodies and NAT, hepatitis B virus antigen and NAT, human T-cell leukemia virus antibodies, syphilis antibodies. Tests for Chagas and

malaria antibodies are performed on some blood products. Tests for HLA antibodies, hemostasis, and residual amotosalen are performed on plasma only.

In 2010, safety was enhanced by pathogen inactivation based on the amotosalen and ultraviolet light process to inactivate pathogens with RNA and DNA. This allows more rapid responses to changes in supply and demand than quarantine. It meets the guidelines of the French health authorities (AFSSAPS) and prevents both known and unknown infection risks (parasites, viruses, bacteria, fungus) and inactivates residual leukocytes. The amotosalen process was chosen because of its relative preservation of fibrinogen compared with other

processes. After amotosalen treatment, plasma is quickly frozen in order to preserve clotting factors. Thereafter, plasma is stored frozen until transfusion or transformation into FLYP. Before lyophilization, amotosalen-treated plasma is selected for factor VIII levels ≥0.96 IU/mL as well as absence of hemolysins or HLA antibodies. This plasma is thawed and pooled (less than 11 different donors per mini-pool). The lyophilization process is performed without any additive solution. The mixed plasma is aseptically filled into glass bottles, according to European good manufacturing practices (clean rooms, air treatment monitoring, sterile water). The lyophilization process is conducted over 6 days.

### Characteristics of FLYP

Comprehensive evaluations were performed to obtain FLYP licensing approval from the AFSSAPS. These studies showed that the lyophilization process does not alter the in vitro hemostatic properties of plasma. During lyophilization, the levels of only two out of nine hemostatic proteins decreased (FV: -25 ± 12%, FVIII: -20 ± 7%), but overall hemostatic efficacy was not affected. Each batch of FLYP produced is specifically tested for hemolysins, unexpected antibodies, factor VIII and fibrinogen, residual Amotosalen, total protein, reconstitution time, and moisture before release (Table 1). FLYP contains all coagulation proteins in physiological concentration ranges as well as albumin and antibodies. Fibrinogen, the key parameter for transfusion during the management of hemorrhagic shock, is almost unchanged compared with fresh plasma and remains stable. The pH upon reconstitution is close to 8. A 50% dilution of FLYP in FWB showed no significant changes in pH of the mixed solution. FLYP is stored at room temperature with a shelf life of 2 years. Its reconstitution takes less than 6 minutes and it is ABO-universal. In

**TABLE 2. In vitro properties of FLYP compared with other French therapeutic plasmas**

Parameters	Units	PFC-SD	PFC-IA	PFC-Se	FLYP	Physiological norms
Fibrinogen	g/L	2.8	2.7	2.8	2.4	2-4
Factor V	IU/mL	0.9	1.0	1.0-1.1	0.7	0.7-1.2
Factor VIII	IU/mL	0.7	0.8	0.9-1.1	0.7	0.5-1.5
Factor XI	IU/mL	0.8	0.6	0.9-1.0	0.7	0.5-1.4
Protein C	IU/mL	1.0	0.9	1.1-1.2	0.9	0.7-1.2
Protein S	IU/mL	0.6	1.0	1.3-1.4	0.9	0.7-1.4
Antithrombin III	IU/mL	0.9	1.0	1.0	1.0	0.8-1.2
$\alpha_2$ antiplasmin	IU/mL	0.2	0.8	1.0	0.9	0.8-1.2

PFC-SD = frozen solvent-detergent plasma; PFC-IA = frozen amotosalen/UV-treated plasma; PFC-Se = frozen secured by quarantine plasma; FLYP = lyophilized amotosalen/UV-treated plasma.

**TABLE 3. Stability of FLYP after reconstitution and storage 24 hours at room temperature and at 4°C**

	Room temperature average of 6 FLYP				4°C average of 6 FLYP			
	T 0	T + 2H	T + 6H	T + 24H	T 0	T + 2H	T + 6H	T + 24H
PT (%)*	70.8	72.0	70.2	60.8	71.2	69.5	64.8	67.2
aPTT (sec)	41.0	42.6	44.1	47.0	41.5	42.9	45.4	45.2
Fibrinogen (g/L)	3.0	2.9	2.9	2.7	3.0	2.9	3.0	2.7
FIXIII (IU/mL)	0.6	0.5	0.5	0.4	0.6	0.5	0.5	0.5
FV (% control)	64.7	63.0	56.2	40.7	65.2	63.0	57.3	40.2

\* The PT% represents test sample prothrombin time plotted against a calibration curve derived from saline dilutions of pooled normal plasma. Results reflect the coagulation activity of the test sample as a percentage of pooled normal, which is 100% by definition.

France, it is regulated as a blood component, and is monitored by the French hemovigilance system, which collects and assesses information on all unexpected or adverse effects. Since 1994, more than 1100 FLYP units have been delivered and no adverse effects have been observed. In particular, no infections or immune reactions have been reported.

### FLYP packaging

FLYP is packaged in a box with: one glass bottle of FLYP powder, a second glass bottle with sterile water for injection, a transfusion kit with vented air intake, a transfer kit, and case report sheets designed for capturing and reporting clinical and laboratory data. For some prehospital use, a new package consisting of a padded bag was developed to facilitate transport of FLYP in a field medical bag.

### In vitro studies of FLYP

The ANSM (Agence nationale de sécurité du médicament et des produits de santé, formerly known as the AFSSAPS, Agency for Sanitary Safety of Health Products) compared concentrations of coagulation proteins in FLYP and other French therapeutic plasmas (Table 2). The results showed no differences.

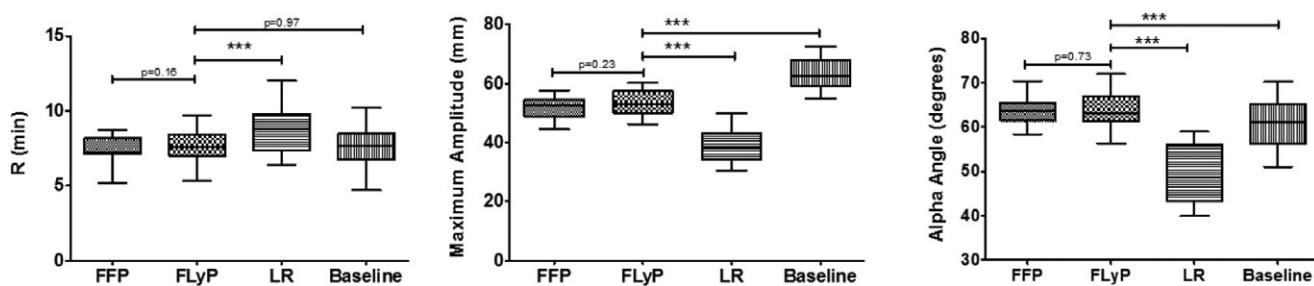
### Stability of FLYP after reconstitution

To test the stability of FLYP, we studied 12 different bottles from the same production batch. After reconstitution, six

bottles were conserved at room temperature and six bottles at 4°C for 24 hours (Table 3). We measured test sample PT against a calibration curve derived from saline dilutions of pooled normal plasma. Results are expressed as PT% and reflect the coagulation activity of the test sample as a percentage of pooled normal (i.e., PT% 50 would be comparable to the coagulation activity remaining after a 1:1 dilution of normal plasma and saline). After 24 hours at 4°C, we observed a minimal reduction of the PT (64.8 % at T + 6H vs. 67.2% at T + 24H), which can be explained by a partial activation of factor VII. Storage at 4°C after reconstitution ensures better preservation of clotting properties than storage at room temperature.

### Dilution model of massive hemorrhage<sup>12</sup>

We designed a dilution model of massive hemorrhage with 40% WB, 30% Lactated Ringer's (LR) solution and either 30% plasma before (FFP) or after lyophilization (FDP). We used both undiluted WB or WB diluted with 60% LR as controls. This model approximates the blood composition of major trauma patients in the first minutes of admission in the emergency room who could receive either LR or FLYP or FWB as resuscitation strategy for massive hemorrhage. We studied all samples by thromboelastography (TEG) and demonstrated that the in vitro hemostatic properties of FLYP were not different from those of the same plasma before lyophilization and were much better than those of LR (Fig. 3). This correction of coagulation impairment was sufficient to trigger clot formation in the same range as undiluted blood. This may



**Fig. 3.** Representation of TEG analyses performed on whole blood of healthy donors. Measurements were performed in blood at baseline (whole blood) and after 60% dilution with Lactated Ringer's solution or after dilution with 30% Lactated Ringer's solution and either 30% plasma before (FFP) or after lyophilization (FLyP). TEG analysis: measurements of R time in seconds (clotting time), alpha angle in degrees (clot kinetic), and maximum amplitude in millimeters (clot firmness). \*\*\*  $p < 0.001$ .

reflect the selection of plasma donors who provide sufficient coagulation factors to induce clot formation even in a hemodiluted state. Thrombin generation assays demonstrated preserved thrombin potential and absence of coagulation factor activation during processing.

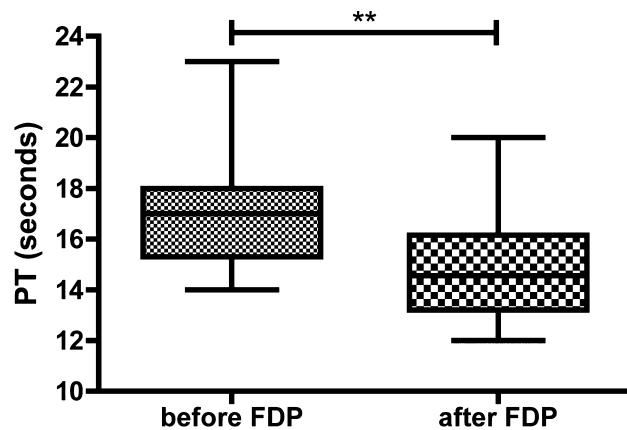
#### Use of FLYP in a French intensive care unit in Afghanistan<sup>13</sup>

The clinical use of FLYP and its effect on PT were assessed in a prospective observational study conducted in a combat environment. This study was conducted from February 2010 to February 2011 at the Kabul Afghanistan International Airport (KAIA) hospital (North Atlantic Treaty Organization [NATO] Role 3), a military treatment facility staffed by an international team including a French intensive care unit with four physicians. Data regarding the clinical safety and efficacy of FLYP in treating trauma-induced coagulopathy were extracted from case report forms filled out by physicians after each FLYP transfusion and reviewed by another physician before statistical analysis. The case report forms captured demographic data, mechanism of injury, physiologic data and vital signs on admission, laboratory tests on admission (hemoglobin, platelet count, fibrinogen level, PT, TEG), and transfusion requirements before administration of FLYP. We studied 87 casualties, of whom 67% were in hemorrhagic shock. Mortality was 10% after 24 hours, and no adverse events from blood products were observed. FLYP was used in accordance with French guidelines. Shock was defined at admission, based on physician findings such as decreased consciousness, pallor, delayed capillary refill, tachycardia ( $>120$  bpm), and hypotension (systolic blood pressure  $< 80$  mmHg).

The predominant mechanisms of injury were gunshot wounds (43%), polytrauma (25%), and explosion (11%). FWB was transfused before FLYP on five occasions (Table 4). The RBC/FLyP ratio transfused was 1:1 (mean = 0.95, 95% confidence interval = [0.79-1.11]), in accordance with the French Armed Forces Health Service resuscitation guidelines. On admission, the mean hemo-

**TABLE 4. Blood products, fluids, and agents given before the use of FLYP**

	Median	Range	% of patients
RBCs (unit)	3	1-13	32
FWB (unit)	4	1-7	5
Crystallloid (L)	1	0.2-5	56
Colloid (L)	0.5	0.1-8	15
Fibrinogen (g)	1.5	1-3	6



**Fig. 4.** Testing of PT before and after FLYP transfusion showed a significant decrease (\*\* $p < 0.01$ ) (box represents mean and 95% confidence interval).

globin level was  $10.1 \pm 2.4$  g/dL, the mean platelet count  $215 \pm 111$  K/ $\mu$ L and the mean fibrinogen level  $2.5 \pm 1.5$  g/L. After administration of FLYP, we observed a significant decrease in PT ( $p < 0.01$ ) with an average decline of 3.3 seconds (from  $20.0 \pm 9.1$  sec to  $16.7 \pm 4.0$  sec) (Fig. 4). Despite active bleeding, we observed stabilization in hemoglobin, platelet count, and fibrinogen levels in response to transfusion therapy and damage control surgery. In summary, our results suggest that FLYP is safe and efficacious for the treatment of coagulopathic combat casualties.

## FUTURE DIRECTIONS

### New reporting

We developed a new, more user-friendly case report form for clinical and laboratory monitoring. Basic clinical data are recorded at admission. Transfusion requirements are monitored. Fibrinogen level and PT are performed before and after administration of FLYP. We also developed new software to report the data and evaluate transfusion practices in overseas operations. Following implementation of this new reporting system, we recorded the following transfusion activity at the KAIA hospital during 2011: 115 patients were transfused with 309 RBC units (range 1-12, mean 2.7 per patient), 93 patients with 303 FLYP units (range 1-14, mean 3.3) and 32 patients with 153 FWB units (range 1-18, mean 4.8). No clearly attributable adverse effects were reported; only two cases of mild erythema were observed without clearly attributable etiology (many drugs were administrated in a short period of time in these critically ill patients).

### New guidelines

For several years, FLYP has been routinely used in strategic air evacuation to France from theaters of operation. We now recommend its early use to prevent coagulopathy in battlefield treatment of severe bleeding at remote NATO Role 1 facilities and in tactical MEDEVAC (e.g., helicopter) of bleeding casualties from Role 1 to Role 2 or 3, before administration of FWB or other blood products. We also propose the use of FLYP in civilian settings to support seriously bleeding patients, before the availability of thawed FFP (within 30 to 90 min of admission) and when the logistical conditions compromise cold chain viability such as for emergency services in extremely isolated locations, mass casualty scenarios, and prehospital settings.

## CONCLUSIONS

From 1945 until now, the CTSA has developed a savoir-faire in the production of FDP and its clinical use. Since 1994, FLYP has been registered as a blood product made from fully tested donor plasma, approved by the ANSM and traced by an active hemovigilance program. No adverse effects associated with its transfusion have ever been observed; in particular, no infections have been reported. FLYP is shelf stable at room temperature, available in less than 6 minutes and is ABO-universal. Since 2010, safety has been augmented by viral inactivation based on the amotosalen-UV illumination process. Since 2012, FLYP has been licensed by the ANSM for civilian use in France, in austere settings or when thawed plasma is unavailable in emergency situations. To date, however, FLYP has been largely used to support overseas operations where, since 2003, the use of more than 1100 FLYP units

was monitored with no adverse events reported. During operations in Africa, FLYP has also been used successfully to prevent or treat bleeding from hemophilia and hemostatic disorders caused by envenomation. In combat casualties, early transfusion of FLYP combined with RBCs, in a 1:1 ratio, appears to provide a survival advantage by prevention or correction of coagulation disorders without adverse effects. These findings require confirmation in a randomized clinical trial. We believe that sufficient data exist to support clinical studies comparing outcomes of resuscitation with FLYP compared with crystalloid in bleeding patients treated in the prehospital setting, and that such studies are indicated.

### ACKNOWLEDGMENTS

We thank the physicians, nurses, and laboratory technicians who provided data from the Intensive Care Unit. We also thank all CTSA workers, anesthesiologists, hemobiologists, and all physicians who work with us on hemorrhagic shock.

### CONFLICT OF INTEREST

For all authors: none disclosures of interest.

## REFERENCES

1. Sailliol A, Ausset S, Peytel E. La transfusion en situation d'exception, expérience du service de santé des armées. *Transfus Clin Biol* 2010;17:279-83.
2. Sailliol A, Ausset S, Martinaud C, Deshayes AV, Massard S, Godier A, Civadier C. Place du plasma cryodesséché dans la prise en charge des hémorragies massives. *Sang Thromb Vaiss* 2011;23:1-7.
3. Daban JL, Clapson P, Ausset S, Deshayes AV, Sailliol A. Freeze dried plasma: a French army specialty. *Crit Care* 2010;14:412.
4. Martinaud C, Tourtier J-P, Pasquier P, Ausset S, Sailliol A. The French freeze dried plasma. Editorial. *J Trauma* 2011; 71:1091-2.
5. Ausset S, Meaudre E, Kaiser E, Sailliol A. Lettre à la rédaction. Prise en charge transfusionnelle du choc hémorragique d'origine traumatique à la phase aiguë : la stratégie du service de santé des armées. *Ann Fr Anesth Reanim* 2009;28:707-9.
6. Ausset S, Meaudre E, Kaiser E, Sailliol A. Transfusion for trauma: the French army policy. *Anaesthesia* 2009;64:1141-51.
7. Agence nationale de sécurité du médicament et des produits de santé. *Transfusion de plasma thérapeutique: produits, indications. Recommandations-Argumentaire.* ANSM-HAS, juin 2012. [cited 2012 Nov 23]. Available from: URL: [http://ansm.sante.fr/var/ansm\\_site/storage/original/application/872563885f6ef900fd735283e334d31e.pdf](http://ansm.sante.fr/var/ansm_site/storage/original/application/872563885f6ef900fd735283e334d31e.pdf).
8. Ausset S, Meaudre E, Sailliol A, Lenoir B. Le facteur VII activé en chirurgie de guerre. Données récentes de la littérature. *Réanoxyo*, 27, octobre 2011.

9. Ausset S, Fevre G, Sailliol A. La transfusion en opérations extérieures militaires. Bull d'hémovigilance 2010;20:6-7.
10. Maurin O, Martinaud C, Boulesteix G, Eve O, Bertrani A, Goudard Y, Kaiser E. Management of bleeding in a child with haemophilia in Africa with freeze-dried plasma. Haemophilia 2012;18:e38-9.
11. Sailliol A, Martinaud C, Civadier C, Deshayes A-V. Mise au point et perspectives sur le plasma lyophilisé. Transfus Clin Biol 2010;17:279-83.
12. Martinaud C, Civadier C, Ausset S, Deshayes AV, Sailliol A. In vitro hemostatic properties of freeze-dried plasma. Anesthesiology 2012;117:339-46.
13. Martinaud C, Ausset S, Deshayes A-V, Cauet A, Demazeau N, Sailliol A. Use of freeze-dried plasma in French intensive care unit in Afghanistan. J Trauma 2011;71:1761-4. 